1631

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Application Number	09/854,847
Filing Date	05/14/01
First Named Inventor	Mathur
Group Art Unit	1631
Examiner Name	C. L. Smith
Attorney Docket Number	LEX-0173-USA

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
- ☐ Fee Attached
- ☒ Amendment/Response
- ☐ After Final
- ☐ Affidavits/declaration(s
- ☒ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
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- ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Lance K. Ishimoto, Reg. No. 41,866 Lexicon Genetics Incorporated
Signature	Peter G Selenan Reg No 40162
Date	February 24, 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Mathur *et al.*	Group Art Unit: 1631	
Application No.:	09/854,847	Examiner: C. L. Smith	
Filed:	05/14/01		
Title:	Novel Human Lipocalin Homologs and Polynucleotides Encoding the Same	Atty. Docket No.: LEX-0173-USA	

#12 Plunkett 3/9/03

AMENDMENT AND RESPONSE TO OFFICE ACTION DATED OCTOBER 30, 2002

Commissioner for Patents
Arlington, VA 22202

Sir:

Applicants acknowledge the receipt of the Office Action ("the Action") mailed on October 30, 2002 (Paper No. 10), which has been carefully reviewed and studied. The Examiner is respectfully requested to enter the following amendments. Reexamination and reconsideration of the application is requested in view of the following amendments and remarks. In order to facilitate the Examiner's evaluation of the application, Applicants have attempted to address the objections and rejections in Paper No. 10 in the same order in which they were originally raised.

A Petition for an Extension of Time of one month to and including February 28, 2003 and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(1) from Applicants' representatives Deposit Account are included. The response is thus timely filed. Applicants believe no fees in addition to the fee for the extension of time are due in connection with this response. However, the Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 50-0892.

AMENDMENT

In the claims:

Please cancel Claim 4 without prejudice or disclaimer as being drawn to a non-elected invention.

Please cancel Claim 1 without prejudice or disclaimer. Please amend Claim 2 to read as follows.

A1

2. (Amended) An isolated nucleic acid molecule comprising a sequence that:

(a) encodes the amino acid sequence of SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the full complement thereof.

Please add new claims 5 and 6.

A2

5. (New) A recombinant expression vector comprising the nucleic acid molecule of claim 3.

6. (New) A cell comprising the expression vector of claim 5.

RESPONSE

I. Status of the Claims

Claim 1 has been cancelled without prejudice or disclaimer. Claim 2 has been amended. Claim 4 has been cancelled without prejudice or disclaimer, as being drawn to a non-elected invention. New claims 5 and 6 have been added. Claims 2-3, 5 and 6 are therefore presently pending in the case. For the convenience of the Examiner and in compliance with 37 C.F.R. § 1.121(c)(1)(ii), a clean copy of the pending claims is attached hereto as **Exhibit A** and a marked-up copy of the original claims is attached hereto as **Exhibit B**

II. Support for the Amended Specification and Claims

Claim 2 has been amended to further clarify the claim, and to recite that the stringent hybridization conditions are highly stringent hybridization conditions. Support for this claim can be

found throughout the specification as originally filed, with particular support being found at least in Claim 2 as originally filed and at page 4, lines 24-30.

New Claim 5 has been added to better claim the present invention. Claim 5 finds support in the sequence listing and throughout the specification as originally filed with particular support being found at least on page 13, line 19-26.

New Claim 6 has been added to better claim the present invention. Claim 6 finds support in the sequence listing and throughout the specification as originally filed with particular support being found at least on page 13, line 26-32.

Amendments to Claim 2 and new claims 5 and 6 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry, therefore, is respectfully requested.

III. Objection

The action objects to Claim 1 for the use of the informality "at" in the claim sentence. Cancellation of Claim 1 eliminates this objection.

IV. Rejection of Claims 1-3 Under 35 U.S.C. § 101

The Action first rejects claims 1-3 under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

The Action seems to be implying that because Applicants' sequence is novel, it lacks utility. Applicants are unaware of any patent law, patent rule, or ruling from the Supreme Court or the Court of Appeals for the Federal Circuit that supports this position.

The Action argues that the present invention lacks "real world" utility that is "specific", "substantial", "credible" or "well-established". Applicants respectfully disagree, in that the present invention has many of these properties and because the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. The PTO has issued numerous patents on polynucleotide sequences that have not been directly shown to be associated with the function of the protein that is set forth in the specification, or a direct association between the

claimed sequences and a particular biological significance, the conditions apparently set forth by the Examiner as allegedly necessary to comply with 35 U.S.C. § 101. The Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,2812 (each of which claims short polynucleotide fragments), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples). None of these issued U.S. Patents contain examples of the "real-world" utilities that the Examiner seems to be requiring in the present Action. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV below), Applicants submit that, logically, the presently claimed invention must also meet the requirements of 35 U.S.C. § 101 and that any other decision is arbitrary and capricious.

Applicants submit that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness

of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. The Examiner states that a "real-world" utility "does not require further research" (Action at page 4). However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need

not disclose what is well known in the art. *In re Wands*, *supra*.

An additional utility of the present invention is in expanding the utility of data coming from the human genome project. Persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. All current therapeutics used in humans directly or indirectly interact with biological sequences encoded by the human genome, and virtually all future human therapeutics shall do likewise. Consequently, billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As just one example of utility of the present nucleotide sequences, Applicants point out that, as taught in the specification as originally filed the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Evidence of the "real world" substantial utility of the present invention is provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Agilent Technologies, Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value (net equity value of the transaction was $620 million) that it was acquired by large pharmaceutical company, Merck & Co., for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. The sequences of the

present invention describe a novel gene encoding a lipocalin like protein and provide a unique identifier of the corresponding gene.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome, as detailed in the specification Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Additionally, since only a small percentage of the genome (2-4%) actually encodes exons, which in-turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications, further discounting the Examiner's position that such uses are "generic". Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

As evidence of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome 9 and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit C**. A blast analysis using the SEQ ID NO:1 of the present invention indicates that the 3 exons encoding the sequence are non-contiguously spread along a region of human chromosome 9 and contained within 2-3 different clones: BC035124, BD027333,

and AL355987, thus clearly one could not simply be able to map the protein encoding regions identified specifically by the sequences of the present invention, without knowing those specific sequences.

For each of the foregoing reasons, Applicants submit that in light of the above discussion the presently claimed invention has a substantial, specific, credible and well-established utility, the rejection of claims 2, 3, 5 and 6 under 35 U.S.C. § 101 has been avoided, and respectfully request that the rejection be withdrawn.

V. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention. Applicants respectfully submit that as pending claims 2, 3, 5 and 6 have been shown to have "a specific, substantial, and credible utility" as detailed in the section above. Applicants therefore request that the rejection of claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. As the action notes the Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*." *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

Although [the applicant] does not have to describe exactly the subject matter claimed,

> ... the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the ... nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of

the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid sequences, or amino acid sequences, of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids, or amino acids, from other materials on the basis of the specific structural description provided. Polynucleotides comprising the nucleotide sequence of , for example, SEQ ID NO:1 or a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:2, are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Thus those of skill in the art would have known how to make and use the invention as claimed in original Claims 2-3. Therefore, Applicants respectfully submit that as Claims 2-3 which read on the full-length sequences are supported by written description in the application (specification and sequences) as originally filed. In fact, the Action (page 7, lines 2-3) states " SEQ ID NO:1 and its full complement of the same length meet the written description provisions of 35 U.S.C. § 112, first paragraph" and on page 8, line 1 " Therefore, only SEQ ID NO:1 encompassed by the claim meets the written description provision of 35 U.S.C. § 112, first paragraph". Clearly, Applicants were in possession of SEQ ID NOS: 1 and 2 at the time the invention was made. The cited statements from the Action signify that the Examiner recognizes that full-length molecules, as described by SEQ ID NOS: 1 and 2, meet the written description provisions of 35 U.S.C. § 112, first paragraph. Thus, Applicants submit that the present claims, which read on full-length molecules, are in compliance with the requirements for written description and respectfully request that the rejection of claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

VII Rejection of Claims 1-3 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claims 1-3 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Action alleges that Claim 1 is indefinite, while Applicant do not agree with this rejection, as Claim 1 has been cancelled, thus this rejection has been rendered moot.

The Action also rejects Claim 2 as allegedly indefinite based on the term "stringent" in regards to hybridization conditions. While Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite "highly stringent" hybridization conditions. As the specification provides specific teaching regarding "highly stringent hybridization conditions", at least at page 4, lines 24-30.

The Action also rejects Claim 2 as allegedly indefinite based on the use of the phrase "the complement thereof". While applicants in no way agree with this rejection, since claim 2 has been revised to read "the full complement thereof", Applicants submit that Claim 2 is sufficiently definite, and respectfully request withdrawal of this rejection.

Finally, the action rejects Claim 3 for recitation of the phrase "encodes *the* amino acid sequence" which the Action claims is vague. Applicants in no way agree, the phrase "encodes *the* amino acid sequence" of SEQ ID NO:2, as in Claim 3, clearly reads on a molecule that encodes the full-length of SEQ ID NO:2.

VII. Rejection of Claims 1-3 Under 35 U.S.C. § 102(e)

The Action next rejects claims 1-3 under 35 U.S.C. § 102(e), as being anticipated by Xu (P/N 6,284,241). Applicants in no way agree with the present rejection.

Claim 1 has been cancelled without prejudice or disclaimer and so its rejection has been rendered moot.

Claim 2 reads on an isolated nucleic acid molecule comprising a sequence that: (a) encodes the amino acid sequence of SEQ ID NO: 2; and (b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the full complement thereof. While it is possible, although

unlikely that the SEQ ID NO:52 of Xu (P/N 6,284,241) might hybridize under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the full complement thereof, it would not encode the amino acid sequence of SEQ ID NO: 2, as the area of commonality contains only 144 residues of SEQ ID NO: 1 and therefore this fragment cannot encode the entire amino acid of SEQ ID NO:2, but only a 48 amino acid fragment thereof. Thus SEQ ID NO:52 of Xu (P/N 6,284,241) cannot properly anticipate the full-length molecules of Claim 2.

Claim 3 reads on an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 2. SEQ ID NO:52 of Xu (P/N 6,284,241) contains a 144 residue fragment of SEQ ID NO: 1 and therefore cannot encode the entire amino acid of SEQ ID NO:2, but only a 48 amino acid fragment thereof, and as such cannot properly anticipate the full-length molecules. Applicants therefore respectfully submit that Xu (P/N 6,284,241) does not properly anticipate claims 1-3 under 35 U.S.C. § 102(e) and respectfully request withdrawal of the rejection.

VIII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Smith have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

Peter G. Seferian
Reg. No. 40162

February 24, 2003
Date

Lance K. Ishimoto Reg. No. No. 41,966
Agent for Applicants

LEXICON GENETICS INCORPORATED
(281) 863-3333

Exhibit A

Clean Version of The Pending Claims in U.S. Patent Application Ser. No. 09/854,847

2. An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the full complement thereof.

3. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

5. (New) A recombinant expression vector comprising the nucleic acid molecule of claim 3.

6. (New) A cell comprising the expression vector of claim 5.

Exhibit B

Marked Up Version of Amended Claims in U.S. Patent Application Ser. No. 09/854,847

1.(Cancelled) An isolated nucleic acid molecule comprising at a nucleotide sequence encoding an amino acid sequence drawn from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 28.

2. An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the full complement thereof.

3. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

4. (Cancelled) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:18.

5. (New) A recombinant expression vector comprising the nucleic acid molecule of claim 3.

6. (New) A cell comprising the expression vector of claim 5.

Home **Paracel BLAST Results** Help

BLASTN 1.2.3-Paracel [2001-11-20]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

Database: month.nt; genbank_update; nt
4,139,212 sequences; 701,142,501,125 total letters

Query=
(555 letters)

Sequences producing significant alignments:	Score (bits)	E Value
BC035124 ACCESSION:BC035124 NID: gi 23958669 gb BC035124.1 Hom...	914	0.0
BD027333 ACCESSION:BD027333 NID: gi 22569075 dbj BD027333.1 Se...	654	0.0
AL355987 ACCESSION:AL355987 NID: gi 20196543 emb AL355987.31 H...	283	2e-73

>BC035124 ACCESSION:BC035124 NID: gi 23958669 gb BC035124.1 Homo sapiens, clone IMAGE:5263500, mRNA
Length = 2905

Score = 914 bits (461), Expect = 0.0
Identities = 461/461 (100%)
Strand = Plus / Plus

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Query: 95   agttctcaggcctctggtacgtggtctccatggcatctgactgcagggtcttcctgggca 154
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2249 agttctcaggcctctggtacgtggtctccatggcatctgactgcagggtcttcctgggca 2308

Query: 155  agaaggaccacctgtccatgtccaccagggccatcaggcccacagaggagggcggcctcc 214
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2309 agaaggaccacctgtccatgtccaccagggccatcaggcccacagaggagggcggcctcc 2368

Query: 215  acgtccacatggagttcccgggggcggacggctgtaaccaggtggatgccgagtacctga 274
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2369 acgtccacatggagttcccgggggcggacggctgtaaccaggtggatgccgagtacctga 2428

Query: 275  aggtgggctccgagggacacttcagagtcccggccttgggctacctggacgtgcgcatcg 334
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2429 aggtgggctccgagggacacttcagagtcccggccttgggctacctggacgtgcgcatcg 2488

Query: 335  tggacacagactacagctccttcgccgtcctttacatctacaaggagctggagggggcgc 394
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2489 tggacacagactacagctccttcgccgtcctttacatctacaaggagctggagggggcgc 2548
```

```
Query: 395  tcagcaccatggtgcagctctacagccggacccaggatgtgagtccccaggctctgaagg 454
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2549 tcagcaccatggtgcagctctacagccggacccaggatgtgagtccccaggctctgaagg 2608


Query: 455  ccttccaggacttctacccgaccctggggctccccgaggacatgatggtcatgctgcccc 514
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 2609 ccttccaggacttctacccgaccctggggctccccgaggacatgatggtcatgctgcccc 2668


Query: 515  agtcagatgcatgcaaccctgagagcaaggaggcgccctga 555
            |||||||||||||||||||||||||||||||||||||||
Sbjct: 2669 agtcagatgcatgcaaccctgagagcaaggaggcgccctga 2709


 Score =  190 bits (96), Expect = 2e-45
 Identities = 96/96 (100%)
 Strand = Plus / Plus


Query: 1    atgatgtcattcctgctcggcgcaatcctgaccctgctctgggcgcccacggctcaggct 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1772 atgatgtcattcctgctcggcgcaatcctgaccctgctctgggcgcccacggctcaggct 1831


Query: 61   gaggttctgctgcagcctgacttcaatgctgaaaag 96
            ||||||||||||||||||||||||||||||||||
Sbjct: 1832 gaggttctgctgcagcctgacttcaatgctgaaaag 1867


>BD027333 ACCESSION:BD027333 NID: gi 22569075 dbj BD027333.1
           Sequence tag and encoded human protein
          Length = 337

 Score =  654 bits (330), Expect = 0.0
 Identities = 334/337 (99%)
 Strand = Plus / Plus


Query: 9    attcctgctcggcgcaatcctgaccctgctctgggcgcccacggctcaggctgaggttct 68
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 1    attcctgctcggcgcaatcctgaccctgctctgggcgcccacggctcaggctgaggttct 60


Query: 69   gctgcagcctgacttcaatgctgaaaagttctcaggcctctggtacgtggtctccatggc 128
            |||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||
Sbjct: 61   gctgcagcctgacttcaatgctgaaaagttctcaggcctctggtacgtggtckccatggc 120


Query: 129  atctgactgcagggtcttcctgggcaagaaggaccacctgtccatgtccaccagggccat 188
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 121  atctgactgcagggtcttcctgggcaagaaggaccacctgtccatgtccaccagggccat 180


Query: 189  caggcccacagaggagggcggcctccacgtccacatggagttcccgggggcggacggctg 248
            |||||||||||||||||||||||||||||||||||||||||||| ||||||||||
Sbjct: 181  caggcccacagaggagggcggcctccacgtccacatggagttcccggggncggacggctg 240
```

```
Query: 249 taaccaggtggatgccgagtacctgaaggtgggctccgagggacacttcagagtcccggc 308
           ||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||
Sbjct: 241 taaccaggtggatgccgagtacctgaaggtgggckccgagggacacttcagagtcccggc 300


Query: 309 cttgggctacctggacgtgcgcatcgtggacacagac 345
           |||||||||||||||||||||||||||||||||||
Sbjct: 301 cttgggctacctggacgtgcgcatcgtggacacagac 337


>AL355987 ACCESSION:AL355987 NID: gi 20196543 emb AL355987.31  Human DNA
            sequence from clone RP11-216L13 on chromosome 9, complete
            sequence
          Length = 182003

 Score =  283 bits (143), Expect = 2e-73
 Identities = 143/143 (100%)
 Strand = Plus / Minus


Query: 95    agttctcaggcctctggtacgtggtctccatggcatctgactgcagggtcttcctgggca 154
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 42496 agttctcaggcctctggtacgtggtctccatggcatctgactgcagggtcttcctgggca 42437


Query: 155   agaaggaccacctgtccatgtccaccagggccatcaggcccacagaggagggcggcctcc 214
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 42436 agaaggaccacctgtccatgtccaccagggccatcaggcccacagaggagggcggcctcc 42377


Query: 215   acgtccacatggagttcccgggg 237
           |||||||||||||||||||||||
Sbjct: 42376 acgtccacatggagttcccgggg 42354


 Score =  216 bits (109), Expect = 3e-53
 Identities = 112/113 (99%)
 Strand = Plus / Minus


Query: 307   gccttgggctacctggacgtgcgcatcgtggacacagactacagctccttcgccgtcctt 366
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 41953 gccttgggctacctggacgtgcgcatcgtggacacagactacagctccttcgccgtcctt 41894


Query: 367   tacatctacaaggagctggaggggcgctcagcaccatggtgcagctctacag 419
           |||||||||||||||||||||||| |||||||||||||||||||||||||||
Sbjct: 41893 tacatctacaaggagctggaggggccctcagcaccatggtgcagctctacag 41841


 Score =  190 bits (96), Expect = 2e-45
 Identities = 96/96 (100%)
 Strand = Plus / Minus
```

```
Query: 1     atgatgtcattcctgctcggcgcaatcctgaccctgctctgggcgcccacggctcaggct 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 42973 atgatgtcattcctgctcggcgcaatcctgaccctgctctgggcgcccacggctcaggct 42914


Query: 61    gaggttctgctgcagcctgacttcaatgctgaaaag 96
             |||||||||||||||||||||||||||||||||||
Sbjct: 42913 gaggttctgctgcagcctgacttcaatgctgaaaag 42878


 Score =  186 bits (94), Expect = 3e-44
 Identities = 100/102 (98%)
 Strand = Plus / Minus


Query: 419   gccggacccaggatgtgagtccccaggctctgaaggccttccaggacttctacccgaccc 478
             |||||||||||||||||||||||||||||||||| ||||||||||||||||||||||
Sbjct: 40774 gccggacccaggatgtgagtccccaggctctgaagtccttccaggacttctacccgaccc 40715


Query: 479   tggggctccccgaggacatgatggtcatgctgccccagtcag 520
             |||||||||||| ||||||||||||||||||||||||||||
Sbjct: 40714 tggggctccccaaggacatgatggtcatgctgccccagtcag 40673


 Score =  143 bits (72), Expect = 4e-31
 Identities = 72/72 (100%)
 Strand = Plus / Minus


Query: 236   gggcggacggctgtaaccaggtggatgccgagtacctgaaggtgggctccgagggacact 295
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 42269 gggcggacggctgtaaccaggtggatgccgagtacctgaaggtgggctccgagggacact 42210


Query: 296   tcagagtcccgg 307
             ||||||||||||
Sbjct: 42209 tcagagtcccgg 42198


 Score = 75.8 bits (38), Expect = 8e-11
 Identities = 38/38 (100%)
 Strand = Plus / Minus


Query: 518   cagatgcatgcaaccctgagagcaaggaggcgccctga 555
             ||||||||||||||||||||||||||||||||||||||
Sbjct: 40341 cagatgcatgcaaccctgagagcaaggaggcgccctga 40304


  Database: month.nt
    Posted date:  Feb 19, 2003  7:16 PM
  Number of letters in database: 232,363,612
  Number of sequences in database:  32,299

  Database: genbank_update
```

```
    Posted date:  Feb 19, 2003  5:25 PM
  Number of letters in database: 100,808,056,008
  Number of sequences in database:  2,556,109

  Database: nt
    Posted date:  Feb 11, 2003  1:41 PM
  Number of letters in database: 600,102,081,505
  Number of sequences in database:  1,550,804

Lambda     K      H
    1.37    0.711     1.31

Gapped
Lambda     K      H
    1.37    0.711     1.31

Matrix: blastn matrix:1 -3
Gap Penalties: Existence: 11, Extension: 1
length of query: 555
length of database: 701,142,501,125
effective HSP length: 21
effective length of query: 534
effective length of database: 701,055,577,673
effective search space: 5108160171078
effective search space used: 5108160171078
T: 0
A: 0
X1: 6 (11.9 bits)
X2: 10 (19.8 bits)
S1: 12 (24.3 bits)
S2: 38 (75.8 bits)
```